Nutritional advantages and disadvantages of dietary phytates: Part 1

Patrice Connelly
B.Nat.Therapies, ADN

KEY MESSAGES

- Phytate a storage form of phosphorus found in plant foods
- Since the 1930s, phytates have been thought of as anti-nutritional factors
- Phytates are known to chelate di- and trivalent cations such as Mg, Ca, Fe, Zn, Cu, Mn and other important minerals needed for health
- In some third-world countries which rely on maize, cassava and plant-based diets, this chelation of minerals has led to malnutrition and other disease states
- More recent research is showing massive benefits of including phytate in the diet, particularly in the area of cancer prevention and treatment (this will be the subject of Part 2 of this article)

INTRODUCTION

Plant foods are an important part of both human and animal diets, but there is much that we still do not understand about them. They provide protein, carbohydrates, fibre, vitamins, minerals, various antioxidants and phytochemicals. Yet those same healthy foods contain components such as phytate, oxalate and tannins which have been called *anti-nutritional* elements.

Phytate, also called phytic acid or myo-inositol hexakisphosphate (IP6 or InsP6) is a storage form of phosphorus which is found in plant-based foods such as grains, legumes and nuts.[1] As a percentage of dry weight, phytates comprise 5.4% of sesame seeds, 2.5% of lima beans, 1.9% of peanuts, 1.4% of soybeans, 1.1% of corn, 1% of barley, 0.9% of wheat and rice, and 0.8% of oats.[2]

Phytate is one source of dietary phosphate for both humans and animals. Since the pioneering work in the 1930s of Harrison and Mellanby on cereal consumption and rickets,[3] research has determined that phytates are responsible for a number of anti-nutritional effects, such as reduction of bioavailability of iron, calcium, selenium, magnesium and other di- and trivalent cations through chelation of these minerals.[3-6] However more recent studies from the 1990s to the present, which will be examined here, have identified a number of health benefits for inclusion of phytate in the diet.

New scientific papers on phytates appear weekly in journals covering a variety of disciplines, from chemistry and biochemistry to plant breeding and human health. However, there appears to be only one comprehensive review of the literature to 2002.[7] Since then, phytate research has progressed significantly; therefore, the aim of this review is to examine the current status of research on phytates, to view the place of phytates in a normal diet, to look at recent findings for new therapeutic roles for dietary phytate, and to assess phytate's synergies with other nutrients such as probiotics.

WHAT ARE PHYTATES?

Myo-inositol hexakisphosphate (IP6) or phytic acid $C_6H_6[OPO(OH)_2]_6$ is an acid found in plant seeds. It is composed of an inositol sugar, similar in structure to D-glucose, with six phosphate groups attached to each hydroxyl branch.[8] Phytate is the salt or ester of phytic acid and is the principal storage form of phosphorus in plant tissues, typically accounting for 60-90% of total seed phosphorus. In a landmark article (cited by over 175 other research papers), Ernst Graf and John Eaton state that it mainly occurs as a mixed Ca-Mg-K salt in discrete areas such as the aleurone layer of wheat and rice.[9] The authors also postulate that the purpose of phytate in plants is to protect the seed against destructive effects of oxygen and iron. In plant cells, phytate helps to regulate calcium and potassium flows, and its complexing ability may help plants to store metal cations.[10]

Phytate is relatively unavailable to humans and monogastric animals that largely lack the enzyme phytase,[11] which is required to degrade phytate. It is also an environmental pollutant in poultry and swine populations, as these animals excrete excess phytate which causes an excess of phosphorus in the local environment. Phytic acid-derived phosphorus in animal waste is a significant contributor to water pollution in the US, Europe and elsewhere.[12]

Research is beginning to uncover important therapeutic functions of the inositol phosphates. IP6 is known to degrade to lower forms of inositol phosphates (IP1-5) which have important roles in human biochemistry as secondary messengers (particularly IP3 and IP6) and in gene expression.[13] Almost all mammalian cells contain IP6 and smaller amounts of the lower inositol phosphates, and inositol occurs in cell membranes in conjunction with lipids as phosphatidylinositol. The inositol phospholipids are important in signal transduction, and they control diverse cellular activities.[14]

DIGESTION OF PHYTATE

Breakdown or degradation of phytate is largely achieved by phytases and phosphatases. In general, phytases can be put into two groups, depending on the initiation site of phosphate hydrolysis in the carbon ring of inositol. Microbial phytases (often fungal) split the carbon bond at C1 or C3, and are known as 3-phytases. Plant phytases act at the C6 position, and are called 6-phytases. Some bacteria such as *Escherichia-coli* also act to break down phytate, but do not fit within these two categories.[15]

A very small amount of phytase activity is present in the small intestine,[16] but most phytate appears to transit the digestive tract relatively intact,[17] with bacterial fermentation occurring largely in the large intestine.[8] Various strategies such as fermentation and germination of phytate-containing foods can release endogenous phytases which begin the phytate breakdown prior to consumption.[18] It is also possible to include specific probiotics such as *Lactobacillus plantarum*, which produces low-level phytase activity.[19]

Bifidobacterium infantis ATCC 15697 is a particular bacterium of interest here, as experiments show a particularly high level of phytate-degrading activity when grown in a Garche broth with 1% lactose, at 37° (100% of IP6, and generating 97.78% IP3 and 2.31% IP4), as well as an enhanced ability to inhibit gastrointestinal pathogens through direct anti-microbial action. Optimum pH for degrading phytate was between 6.0 and 6.5. As this is the dominant human colonic bacteria during the first year of life, it has obvious survival benefits and protection for newborns, but it is also known to stimulate synthesis of immuno-modulating molecules such as IL-10, IL-12 and TNF-α.[20] Several forms of bifidobacteria were studied, with results showing that *B. longum* ATCC 15707 achieved a 12% hydrolysis of IP6, plus generation of lower inositol phosphates at levels of 0.41% IP5, 2.02% IP4 and 1.08% IP3. Other bifidobacteria tested showed lesser or no activity.

THE ANTI-NUTRITIONAL FACTOR

The anti-nutritional aspect of phytate occurs due to the complexing action of phytate on other di- and trivalent cations, namely Cu, Zn, Ni, Co, Mn, Fe, Se, Mg and Ca. Graf and Eaton explain that one phytate molecule can bind up to six divalent cations, and the metal ion may bridge at least two phytate molecules, depending on the redox state.[9] They note that the effect of this chelation on the bioavailability of minerals depends on the ratio of metal-to-phytate, and the number of different cations which are in the complex. The more cations included, the more insoluble the complex.

This anti-nutritional aspect of phytates has been the focus of many research papers. Many of these studies have looked at the effects of mineral deficiencies on various populations – infants,[21,22] children,[23] adolescents,[24] and adults,[25] and propose ways of overcoming these problems.

The problems of mineral chelation and subsequent deficiencies are real. Deficiencies of iron and zinc can cause anaemia, poor psychomotor development, impaired growth and increased risk of diarrhoea and respiratory infections.[21] Other minerals are also involved with serious health consequences in deficiency states. Some studies have looked at the effects of phytate-reduced foods, while others concentrate on interactions between phytate and different methods of fortifying foods.

It appears that not all plant foods containing phytate may promote iron deficiency. Soybeans particularly, and legumes in general have a high iron content, and much of it is in the form of ferritin, the storage form of iron. In the case of soybeans, it is approximately 90% ferritin, whereas in wheat grain, the iron is complexed to phytate as monoferricphytate which is unavailable for absorption.[26] Ferritin iron is contained in a protein coat and researchers suggest it is likely that ferritin-bound iron is less sensitive to phytate chelation, and is therefore more bioavailable.[27]

A study which examined calcium absorption from white and red and pinto beans demonstrated that the bioavailability of calcium was far less than from milk. However, the authors looked at a past study which showed that calcium was more bioavailable from soybeans, and they suggest that common beans may include an extra inhibitor other than phytate which is not present in soybeans.[28]

Some researchers have tested the use of Vitamin A and β-Carotene to improve iron absorption from phytate-rich foods. One study showed that both substances increase iron absorption by significant amounts. The mechanism appears to work because vitamin A creates a complex with phytate's binding sites, reducing the chelation effect, and making iron more soluble.[29]

Other researchers have looked at a variety of fortification substances, such as ascorbic acid, [30] iron-EDTA and iron bis-glycine chelate,[31] citric acid[32] and dairy products.[33] While results of studies of ascorbic acid on iron absorption were mixed, one study found that 30 mg of ascorbic acid can counteract between 10-58 mg of phytate, though a greater amount (50 mg or more) of ascorbic acid may be needed if the food is also high in tannins.[30] This is in contrast to a later study by Hunt et al who found that ascorbic acid at levels of 500 mg t.i.d. did not appear to increase iron absorption.[34] Further research into the optimum levels for this particular role of ascorbic acid may be required.

Fortification of grains with different iron chelates has shown mixed results, with one study of NaFeEDTA fortification of wheat and soy foods concluding that NaFeEDTA does not provide any nutritional benefit compared with the combination of a highly bioavailable iron compound and ascorbic acid.[22] But the compound

iron bis-glycine chelate, in the form of Ferrochel, was tested in 74 adults, and found effective in preventing iron deficiency.[31]

A study of phytase and citric acid supplementation in whole-wheat bread was also found to produce positive results in improving phosphorus and iron bioavailability. The citric acid at an amount of 6.25g/kg of flour produced significant degradation of phytate, creating a more acid bread dough.[32] However, adding milk to a plant-based diet does not appear to have the same results for improving iron availability although it does improve zinc uptake, with one study finding an improvement in zinc absorption of 70%.[33,35]

Further research into the anti-nutritional aspects of phytates has concluded that the best way to deal with phytate and prevent mineral deficiencies is to reduce the amount of phytate in grains. Corn, barley, rice and soybeans have naturally occurring low phytic acid (lpa) mutants which block the ability of a seed to synthesise phosphorus into phytic acid, but still have normal levels of phosphorus. The reductions can range from 50% to over 90%, and show increases either in inorganic phosphorus and/or myo-inositol phosphates with five or fewer P groups.[12]

Spelt, the ancient form of wheat, has shown a naturally lower phytate content. One study showed that even though phosphorus content was higher in spelt than in wheat brans, phytic acid content showed the opposite trend and was 40% lower in spelt versus wheat fine bran, which may suggest that spelt has either a higher endogenous phytase activity or a lower phytic acid content than wheat. The results of this study give important indications on the real nutritional value of spelt compared to wheat.[36]

Genetic modification of plants to reduce phytate content is also prevalent. An example of this research where *Arabidopsis thaliana* (a small flowering plant related to cabbage and mustard) was used as a model organism, found that the disruption of the two kinases responsible for phytate synthesis have resulted in a significant reduction in phytate content, without affecting the normal yield of phosphorus and seed.[11]

The development of low-phytate crops is of considerable importance to agriculture, because excretion of phytate is an environmental pollutant. However, not all of this research is directed at animals. Where phytate has proven to be an antinutrient, particularly in third world countries, the introduction of low-phytate crops, both hybrid and genetically modified, is being suggested by many researchers. Research since the 1980s has shown a number of human health benefits for phytate, despite its effects on nutrient status, and this will be the focus of the next section.

Part 2 will be published in the June edition of JATMS.

REFERENCES

1. Gropper, S.S., J.L. Smith, and J.L. Groff, *Advanced nutrition and human metabolism*. 4th ed. 2005, Belmont, CA: Thomson Wadsworth.
2. Graf, E. and J.W. Eaton, *Suppression of colonic cancer by dietary phytic acid*. Nutr Cancer, 1993. 19(1): p. 11-19.
3. Harrison, D.C. and E. Mellanby, *Phytic acid and the rickets-producing action of cereals*. Biochemical Journal, 1939. 33(10): p. 1660-1680.
4. Cruikshank, E.W.H., et al., *The digestibility of the phytic acid of oatmeal in adult man*. Journal of Physiology, 1945. 104(1): p. 41-46.
5. Bronner, F., et al., *Studies in calcium metabolism. Effect of food phytates on calcium uptake in boys on a moderate calcium breakfast*. Journal of Nutrition, 1956. 59(3): p. 393-406.
6. James, W.P., W.J. Branch, and D.A. Southgate, *Calcium binding by dietary fibre*. Lancet, 1978. 1(8065): p. 638-9.
7. Fox, C.H. and M. Eberl, *Phytic acid (IP6), novel broad spectrum anti-neoplastic agent: a systematic review*. Complement Ther Med, 2002. 10(4): p. 229-34.
8. Steer, T.E. and G.R. Gibson, *The microbiology of phytic acid metabolism by gut bacteria and relevance for bowel cancer*. International Journal of Food Science and Technology, 2002. 37: p. 783-790.
9. Graf, E. and J.W. Eaton, *Antioxidant functions of phytic acid*. Free Radical Biology & Medicine, 1990. 8: p. 61-69.
10. Veiga, N., et al., *The Behaviour of myo-Inositol Hexakisphosphate in the Presence of Magnesium(II) and Calcium(II): Protein-Free Soluble InsP6 is Limited to 49 μM under Cytosolic/Nuclear Conditions*. Journal of Inorganic Chemistry, 2006. 100(11): p. 1800-1810.
11. Stevenson-Paulik, J., et al., *Generation of phytate-free seeds in Arabidopsis through disruption of inositol polyphosphate kinases*. Proceedings of the National Academy of Science, USA, 2005. 102(35): p. 12612-7.
12. Raboy, V., *Progress in breeding low phytate crops*. J Nutr, 2002. 132(3): p. 503S-505S.
13. Shen, X., et al., *Modulation of ATP-dependent chromatin-remodeling complexes by inositol polyphosphates*. Science, 2003. 299(5603): p. 112-114.
14. Vucenik, I. and A.M. Shamsuddin, *Cancer inhibition by inositol hexaphosphate (IP6) and inositol: from laboratory to clinic*. J Nutr, 2003. 133(11 Suppl 1): p. 3778S-3784S.
15. Lei, X.G. and J.M. Porres, *Phytase enzymology, applications, and biotechnology*. Biotechnol Lett, 2003. 25(21): p. 1787-94.
16. Iqbal, T.H., K.O. Lewis, and B.T. Cooper, *Phytase activity in the human and rat small intestine*. Gut, 1994. 35: p. 1233-1236.
17. Sandberg, A.S. and H. Andersson, *Effect of dietary phytase on the digestion of phytate in the stomach and small intestine of humans*. J Nutr, 1988. 118(4): p. 469-73.
18. Svanberg, U., W. Lorri, and A.S. Sandberg, *Lactic fermentation of non-tannin and high-tannin cereals: effects on in vitro estimation of iron availability and*

phytate hydrolysis. Journal of Food Science, 1993. 58(2): p. 408-412.

19. Zamudio, M., A. Gonzalez, and J.A. Medina, *Lactobacillus plantarum phytase activity is due to non-specific acid phospatase.* Letters in Applied Microbiology, 2001. 32: p. 181-184.

20. Haros, M., et al., *Myo-inositol hexakisphosphate degradation by Bifidobacterium infantis ATCC 15697.* Int J Food Microbiol, 2007. 177: p. 76-84.

21. Lind, T., et al., *Effects of weaning cereals with different phytate content on growth, development and morbidity: a randomized intervention trial in infants from 6 to 12 months of age.* Acta Paediatr, 2004. 93(12): p. 1575-82.

22. Davidsson, L., et al., *Sodium iron EDTA [NaFe(III) EDTA] as a food fortificant: erythrocyte incorporation of iron and apparent absorption of zinc, copper, calcium, and magnesium from a complementary food based on wheat and soy in healthy infants.* Am J Clin Nutr, 2005. 81(1): p. 104-9.

23. Andang'o, P.E.A., et al., *Efficacy of iron-fortified whole maize flour on iron status of schoolchildren in Kenya: a randomised controlled trial.* The Lancet, 2007. 369(9575): p. 1799-1806.

24. Gibson, R.S., A.-L.M. Heath, and E.L. Ferguson, *Risk of suboptimal iron and zinc nutriture among adolescent girls in Australia and New Zealand: causes, consequences, and solutions.* Asia Pac J Clin Nutr, 2002. 11 (Suppl 3): p. S543-52.

25. Kohlmeier, L., et al., *Deficient dietary iron intakes among women and children in Russia: evidence from the Russian Longitudinal Monitoring Survey.* American Journal of Public Health, 1998. 88(4): p. 576-580.

26. Murray-Kolb, L.E., et al., *Women with low iron stores absorb iron from soybeans.* American Journal of Clinical Nutrition, 2003. 77: p. 180-184.

27. Bejjani, S., et al., *Gastric digestion of pea ferritin and modulation of its iron bioavailability by ascorbic and phytic acids in caco-2 cells.* World J Gastroenterol, 2007. 13(14): p. 2083-8.

28. Weaver, C.M., et al., *Absorbability of calcium from common beans.* Journal of Food Science, 1993. 58(6): p. 1401-1403.

29. Garcia-Casal, M., et al., *Vitamin A and B-carotene can improve nonheme iron absorption from rice, wheat and corn by humans.* Journal of Nutrition, 1997. 128(3): p. 646-650.

30. Siegenberg, D., et al., *Ascorbic acid prevents the dose-dependent inhibitory effects of polyphenols and phytates on nonheme-iron absorption.* American Journal of Clinical Nutrition, 1991. 53(2): p. 537-41.

31. Layrisse, M., et al., *Iron bioavailability in humans from breakfasts enriched with iron bis-glycine chelate, phytates and polyphenols.* J Nutr, 2000. 130(9): p. 2195-9.

32. Porres, J.M., et al., *Phytase and citric acid supplementation in whole-wheat bread improves phytate-phosphorus release and iron dialyzability.* Journal of Food Science, 2001. 66(4): p. 614-619.

33. Rosado, J.L., et al., *The addition of milk or yogurt to a plant-based diet increases zinc bioavailability but does not affect iron bioavailability in women.* J Nutr, 2005. 135(3): p. 465-8.

34. Hunt, J.R., S.K. Gallagher, and L.K. Johnson, *Effect of ascorbic acid on apparent iron absorption by women with low iron stores.* American Journal of Clinical Nutrition, 1994. 59(6): p. 1381-1385.

35. Hurrell, R.F., et al., *Degradation of phytic acid in cereal porridges improves iron absorption by human subjects.* Am J Clin Nutr, 2003. 77(5): p. 1213-9.

36. Ruibal-Mendieta, N.L., et al., *Spelt (Triticum aestivum ssp. spelta) as a source of breadmaking flours and bran naturally enriched in oleic acid and minerals but not phytic acid.* J Agric Food Chem, 2005. 53(7): p. 2751-9.